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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,558	12/06/2000	Ronald R. Marquardt	3027 .00014	8576

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	16

DATE MAILED: 08/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/673,558	MARQUARDT et al.
Examiner	**Art Unit**
James L. Grun, Ph.D.	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *9 Jun 2003*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-5, 8, 9, and 12-21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5, 8, 9, and 12-21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

The amendment filed 09 June 2003 is acknowledged and has been entered. Claims 6, 7, 10, and 11 have been cancelled. Claims 1-5, 8, 9, and 12-21 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 3, 8, and 9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, "lable" should be --label--.

In claims 8 and 9, "the biomolecule" lacks antecedent basis.

Claims 12, 14-18, and 20-21 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Behnke et al (U.S. Pat. No. 5,573,921) for reasons of record.

Claims 12-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Marquardt et al (WO 97/43438), Eibl et al (U.S. Pat. No. 4,276,259), Fish et al (U.S. Pat. No. 5,126,276), and Köhler (U.S. Pat. No. 4,822,565) for reasons of record.

Applicant's arguments filed 09 June 2003 have been fully considered but they are not deemed to be persuasive. Applicant urges that certain limitations distinguish the claims over the cited prior art because the prior art references teach additional steps, such as washing steps, in their methods. This is not found persuasive because applicant's arguments are drawn to limitations not found in the instantly rejected claims. Notwithstanding applicant's assertions to the contrary, no amendments have been made to enter any of the argued limitations into the instantly rejected claims and the instant open claim language does not exclude any additional steps.

Claims 1-5, 8, 9, and 12-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piasio et al. (U.S. Pat. No. 4,225,575) in view of Ryan et al. (U.S. Pat. No. 4,115,374).

Piasio et al. teach a method and apparatus for conducting a chemical, enzymatic, or immunochemical reaction wherein one or more of the reactants is/are affixed to the surface of an immersible solid phase matrix and one or more other reactants is/are freely diffusible in a liquid reaction medium in which the solid phase matrix is immersed. The solid phase matrix is of a shape constructed as to provide a large surface area, a short transfer distance for the mobile reactants, and free drainage from the surface upon removal from the liquid reaction medium (e.g. col. 7, lines 30-43), and is depicted variously as star-shaped, as pins, as a cylinder, or as a spiral (e.g. Figs. 1-6). The reaction is carried out in a reaction vessel such as a tube, is readily initiated by immersing the solid phase matrix into the vessel holding the liquid reaction medium

containing the freely mobile reactant(s), and is stopped by removing the solid phase matrix therefrom. Thereby the invention achieves the advantages of, inter alia, eliminating timing errors in starting and stopping reactions, facilitating separation of reaction components and products and/or solid and liquid phases, and eliminating washing steps compared to prior assays using alternatives such as coated tubes (e.g.: col. 4, lines 3-6 and 24-29; col. 7, lines 44-48; col. 10, lines 38-57; col. 11, lines 19-27). After removal of the solid phase, if desired, it can be transferred directly to a measurement device (e.g. col. 8, lines 31-46). Quantitative results are obtained by measuring the formation of products or disappearance of reactants in enzyme-catalyzed reactions or by measuring the amount of mobile component bound or unbound in immunochemical reactions (e.g.: col. 1, lines 20-40; claims 1-7). In one embodiment, the mobile component can be an enzyme of clinical significance in a sample of biological material and the component fixed to the solid phase matrix can be a substrate for the enzyme (e.g.: col. 3, lines 8-18; claims 1 and 7). For example, radiolabelled *Micrococcus lysodeikticus* can be bound to the surface of the solid phase matrix for performing a lysozyme assay. *Micrococcus lysodeikticus* is a notoriously old and well known substrate for lysozyme. Further, the assay of Ryan et al. is specifically suggested as an example of another such assay for enzyme activity adaptable for use with the method and apparatus of the reference of Piasio et al wherein enzyme substrate is affixed to the solid phase matrix. In contrast to the invention as instantly claimed, the reference does not specifically teach the manner of measurement used for the specifically suggested enzyme assays.

Ryan et al. teach radiolabelled substrates for assays of angiotensin converting enzyme (ACE) in samples of biological material with or without addition of enzyme inhibitors to the samples. The radiolabel is incorporated into that portion of the substrate which becomes the remnant product cleaved from the substrate by the activity of the enzyme. In contrast to the invention as instantly claimed the assay of Ryan et al. does not involve a solid phase fixed reagent nor the separation of reagents and products by removal of the solid phase.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used labelled enzyme substrates affixed to the solid phase for assays of enzymatic activity in biological samples, such as using the labelled substrates of Ryan et al. for ACE assays with or without enzyme inhibitors or using labelled *Micrococcus lysodeikticus* for lysozyme assays, with the apparatus and method of Piasio et al. motivated by the direct suggestion in the reference to do so. One would have had an extremely reasonable expectation of successfully detecting the activity of such enzymes in assays of such design by measuring the release of labelled remnant products into the reaction medium or the disappearance of labelled substrate from the solid phase matrix in the enzyme-catalyzed reactions as is conventional in the art and readily apparent to one of ordinary skill in the art as a matter of design choice from the design of the suggested assays of Piasio et al.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 1-5, 8, 9, and 12-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Marquardt et al. (WO 97/43438), Piasio et al. (U.S. Pat. No. 4,225,575), and Ryan et al. (U.S. Pat. No. 4,115,374).

Marquardt et al. teach solid phase assays, both competitive and non-competitive, for bioactive substances, including enzymes and their inhibitors, essentially as instantly disclosed using a first labelled component bound to the solid phase and a second component, which reacts with the first component, in the sample contacted with the solid phase except for the assays being performed in microtiter plates as the solid phase rather than on an insertable solid phase.

The teachings of Piasio et al. (U.S. Pat. No. 4,225,575) and Ryan et al. (U.S. Pat. No. 4,115,374) are as set forth previously.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted the insertable solid phase known to the art, as taught in Piasio et al. in view of Ryan et al., for the microtiter plates in the assays of Marquardt et al. because Piasio et al. in view of Ryan et al. teach assays identical in design to those taught in Marquardt et al. wherein a first labelled component bound to the solid phase reacts with a second component in the sample which is being assayed and one would have been motivated to make the substitution because Piasio et al. specifically teaches the insertable solid phase matrix as an alternative to coated reaction vessels such as coated tubes for the benefits taught specifically therein such as eliminating timing errors in starting and stopping reactions, facilitating separation

of reaction components and products and/or solid and liquid phases, and eliminating washing steps.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (703) 308-3980. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (703) 305-3399.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306, or (703) 305-3014, or (703) 308-4242. Official After Final communications, only, can be facsimile transmitted to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. The above inquiries, or requests to supply missing elements from Office communications, can also be directed to the TC 1600 Customer Service Office at phone numbers (703) 308-0197 or (703) 308-0198.

James L. Grun, Ph.D.
August 21, 2003

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641